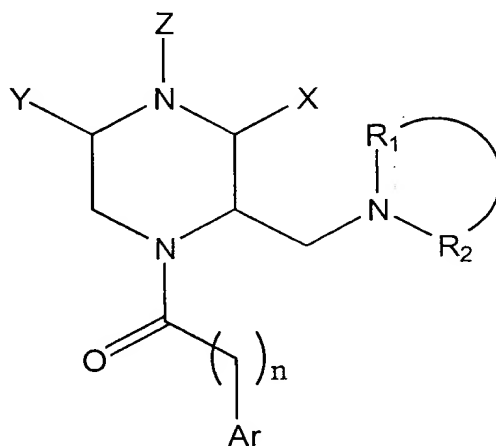


WHAT IS CLAIMED IS:

1. A pharmaceutical composition for the prevention or treatment of pruritus comprising a compound of formula I or a pharmaceutically acceptable salt thereof



(I)

wherein

 $n = 1-3$; R_1 and R_2 are independently $= \text{CH}_3$; $-(\text{CH}_2)_m$, where $m =$ 4-8, $-\text{CH}_2\text{CH}(\text{OH})(\text{CH}_2)_2-$; $-\text{CH}_2\text{CH}(\text{F})(\text{CH}_2)_2-$; $-(\text{CH}_2)_2\text{O}(\text{CH}_2)_2-$; or $-(\text{CH}_2)_2\text{CH}=\text{CHCH}_2-$; $\text{Ar} =$ unsubstituted or mono-, or di-substituted phenyl

wherein said substituents are selected from the group

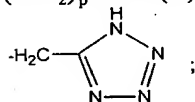
consisting of halogen, OCH_3 , SO_2CH_3 , CF_3 , amino, alkyl,

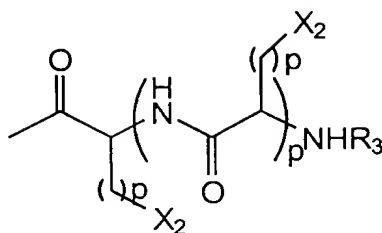
and 3,4-dichloro; benzothiophenyl; benzofuranyl; naphthyl;

diphenyl methyl; or 9-fluorene;

 Z is

$-\text{P}(\text{O})(\text{OBn})_2$; $-\text{P}(\text{O})(\text{OH})_2$; $-(\text{CH}_2)_p\text{C}(\text{O})\text{NHOH}$; $-(\text{CH}_2)_p\text{CO}_2\text{H}$; $-\text{SO}_2\text{CH}_3$; $-\text{SO}_2\text{NH}_2$;
 $-\text{CO}(\text{CH}_2)_p\text{CH}(\text{NH}_2)(\text{CO}_2\text{H})$; $-\text{COCH}(\text{NH}_2)(\text{CH}_2)_p\text{CO}_2\text{H}$; $-\text{CO}_2\text{CH}_3$; $-\text{CONH}_2$;
 $-(\text{CH}_2)_p\text{O}(\text{CH}_2)_p\text{CO}_2\text{H}$; $-(\text{CH}_2)_p\text{O}(\text{CH}_2)_p\text{CONHOH}$; $-(\text{CH}_2)_p\text{NH}\text{SO}_2\text{CH}_3$; $-(\text{CH}_2)_p\text{NHC}(\text{S})\text{NHCH}(\text{CO}_2\text{H})(\text{CH}_2)_p\text{CO}_2\text{H}$; $-(\text{CH}_2)_p\text{SO}_3\text{H}$; or

or Z is

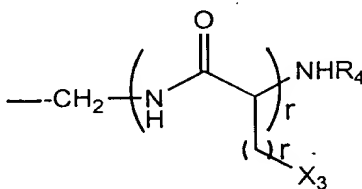


wherein

$p = 0-20$;
 $R_3 = -H$ or $-Ac$;
 $X_2 = -CO_2H$; $-NHSO_2CH_3$; $NHP(O)(OBn)_2$; $NHP(O)(OH)_2$;
 $-OP(O)(OBn)_2$; or $OP(O)(OH)_2$;

X and Y are independently

$-CH_2NHSO_2CH_3$, $-CH_2NHP(O)(OBn)_2$, $-CH_2NHP(O)(OH)_2$, $-CH_2OP(O)(OBn)_2$,
 $-CH_2OP(O)(OH)_2$, $-(CH_2)_qO(CH_2)_qCO_2H$, $-(CH_2)_qO(CH_2)_qSO_3H$,
 $-(CH_2)_qO(CH_2)_qCHNHOH$,
 $-CH_2NHC(S)NHCH(CO_2H)(CH_2)_qCO_2H$, or



wherein

$q = 1-20$
 $r = 1-20$
 $R_4 = -H$ or $-Ac$
 $X_3 = -CO_2H$; $-NHSO_2CH_3$; $-NHP(O)(OBn)_2$;
 $-NHP(O)(OH)_2$; $-OP(O)(OBn)_2$; or
 $-OP(O)(OH)_2$

in a pharmaceutically acceptable carrier.

2. The pharmaceutical composition according to claim 1 wherein said compound is
 selected from the group consisting of: {4-[1-(3,4-Dichlorophenyl)acetyl-2R-(1-pyrrolidinyl)-
 methyl]piperazinyl} acetic acid; [1-(3,4-Dichlorophenyl)acetyl-4-methanesulfonyl-2R-(1-
 pyrrolidinyl)methyl]piperazine; [4-S-Aspartic acid- α -amido-1-(3,4-dichlorophenyl)acetyl-
 2R-(1-pyrrolidinyl)methyl]piperazine; Methyl-[2R-(O-2-acetic acid)hydroxymethyl-4-(3,4-
 dichlorophenyl)acetyl-3R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[2R-(O-
 S-aspartic acid- α -acetyl)hydroxymethyl-4-(3,4-dichlorophenyl)acetyl-3R-(1-
 pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[4-(3,4-dichlorophenyl)acetyl-2R-(N-

methanesulfonamido)aminomethyl-3R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-{4-[3,4-dichlorophenyl]acetyl-3R-[1-pyrrolidinyl)methyl-2R-[N-(succinic acid-2S-thioureido)]aminomethyl}-1-piperazinecarboxylate; Methyl-[2S-(O-2-acetic acid)hydroxymethyl-4-(3,4-dichlorophenyl)acetyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[2S-(O-S-aspartic acid- α -acetyl)hydroxymethyl-4-(3,4-dichlorophenyl)acetyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[4-(3,4-dichlorophenyl)acetyl-2S-(N-methanesulfonamido)aminomethyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-{4-[3,4-dichlorophenyl]acetyl-5R-[1-pyrrolidinyl)methyl-2S-[N-(succinic acid-2S-thioureido)]aminomethyl}-1-piperazinecarboxylate; Methyl-[2R-(O-2-acetic acid)hydroxymethyl-4-(3,4-dichlorophenyl)acetyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[2R-(O-S-aspartic acid- α -acetyl)hydroxymethyl-4-(3,4-dichlorophenyl)acetyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; Methyl-[4-(3,4-dichlorophenyl)acetyl-2R-(N-methanesulfonamido)aminomethyl-5R-(1-pyrrolidinyl)methyl]-1-piperazinecarboxylate; and Methyl-{4-[3,4-dichlorophenyl]acetyl-5R-[1-pyrrolidinyl)methyl-2R-[N-(succinic acid-2S-thioureido)]aminomethyl}-1-piperazinecarboxylate.

3. The pharmaceutical composition according to claim 1 wherein said compound is selected from the group consisting of:

(*R*)-4-(Phenylmethyl)-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]piperazine hydrochloride;

(*R*)-1-[(3,4-Dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]piperazine hydrochloride;

(*R*)-4-Methanesulfonyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

(*R*)-4-*t*-Butyl-acetyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine;

(*R*)-4-[(3,4-Dichlorophenyl)acetyl]-3-[(1-pyrrolidinyl)methyl]-1-piperazineacetic acid dihydrochloride;

(*R*)-4- N-*t*-Boc-D-aspartic acid- β -benzyl ester-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine;

(*R*)-4-Aspartic acid-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine dihydrochloride;

(*R*)-4-Acetyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

(R)-4-(Diethoxyphosphonate)-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

5 (R)-4-Trifluoroacetyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

(R)-4-[(3,4-Dichlorophenyl)acetyl]-3-[(1-pyrrolidinyl)methyl]-1-piperazinecarboxamide hydrochloride;

10 (R)-4-[(3,4-Dichlorophenyl)acetyl]-3-[(1-pyrrolidinyl)methyl]-1-piperazinecarboxaldehyde hydrochloride;

15 (R)-4-[(3,4-Dichlorophenyl)acetyl]-3-[(1-pyrrolidinyl)methyl]-1-piperazine-sulfonamide hydrochloride;

(R)-4-(4-Methylphenylsulfonyl)-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

20 (R,S)-4-Methanesulfonyl-1-[(3,4-dichlorophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]-piperazine hydrochloride;

(R,S)-4-Methanesulfonyl-1-[(4-methylsulfonylphenyl)acetyl]-2-[(1-pyrrolidinyl)-methyl]piperazine hydrochloride;

25 (R,S)-4-Methanesulfonyl-1-[(2-nitrophenyl)acetyl]-2-[(1-pyrrolidinyl)-methyl]piperazine hydrochloride;

30 (R,S)-4-Methanesulfonyl-1-[(4-trifluoromethylphenyl)acetyl]-2-[(1-pyrrolidinyl)-methyl]piperazine hydrochloride;

(R,S)-4-Methanesulfonyl-1-[(3-indolylacetyl)-2-[(1-pyrrolidinyl)-methyl]piperazine hydrochloride;

35 (R,S)-Methyl 4-[(4-methylsulfonylphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazinecarboxylate hydrochloride;

(R,S)-Methyl 4-[(4-trifluoromethylphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazinecarboxylate hydrochloride;

40 (R,S)-Methyl 4-[(3-indolyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazine-carboxylate hydrochloride;

45 (R,S)-Methyl 4-[(2-nitrophenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazine-carboxylate hydrochloride;

(R,S)-Methyl 4-[(2-methoxyphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazine-carboxylate hydrochloride;

(*R,S*)-Methyl 4-[(2-aminophenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-1-piperazine-carboxylate dihydrochloride;

5 (*R,S*)-4-Acetyl-1-[(4-methylsulfonylphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]-piperazine hydrochloride;

(*R,S*)-4-Acetyl-1-(4-trifluoromethylphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl] piperazinecarboxylate hydrochloride;

10 (*R,S*)-4-Acetyl-1-[(2-trifluoromethylphenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl] piperazinecarboxylate hydrochloride;

15 (*R,S*)-4-Acetyl-1-[(3-nitrophenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]piperazine-carboxylate hydrochloride;

(*R,S*)-4-Acetyl-1-[(2-nitrophenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]piperazine-carboxylate hydrochloride;

20 (*R,S*)-4-Acetyl-1-[(4-nitrophenyl)acetyl]-3-[(1-pyrrolidinyl)-methyl]piperazine-carboxylate hydrochloride; and

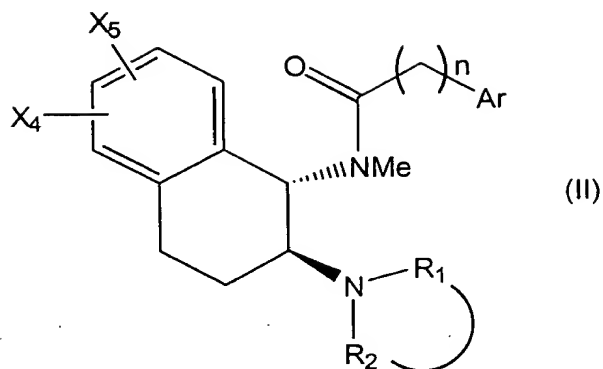
(*R,S*)-4-(Phenylmethyl)-1-[(4,5-dichloro-2-nitrophenyl)acetyl]-2-[(1-pyrrolidinyl)methyl]piperazine dihydrochloride.

25 4. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 1.

30 5. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 2.

6. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 3.

35 7. A pharmaceutical composition for the prevention or treatment of pruritus comprising a compound of formula II or a pharmaceutically acceptable salt thereof



wherein

$n = 1-3$;

R_1 and R_2 are independently $= CH_3$; $-(CH_2)_m$, where $m = 4-8$, $-CH_2CH(OH)(CH_2)_2$; $-CH_2CH(F)(CH_2)_2$; $-(CH_2)_2O(CH_2)_2$; or $-(CH_2)_2CH=CHCH_2$;

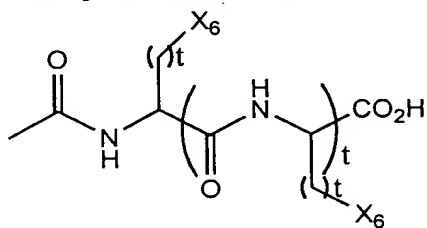
Ar = unsubstituted or mono-, or di-substituted phenyl wherein said substituents are selected from the group consisting of halogen, OCH_3 , SO_2CH_3 , CF_3 , amino, alkyl, and 3,4-dichloro; benzothiophenyl; benzofuranyl; naphthyl; diphenyl methyl; or 9-fluorene;

X_4 and X_5 are independently

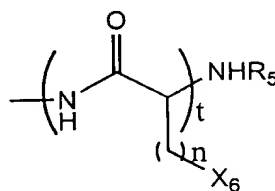
$-OP(O)(OBn)_2$; $-OP(O)(OH)_2$; $-CO_2H$; $-SO_3H$; $-SO_3H$; $-O(CH_2)_nCO_2H$; $-NHCO_2CH_3$; $-CONH(CH_2)_sCO_2H$; or $-SO_2NH(CH_2)_sCO_2H$; wherein

$s = 1-5$

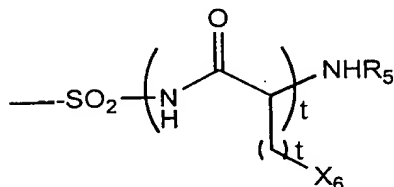
or X_4 and X_5 are independently



; or



; or



wherein

t = 1-20

R₅ = -H or -Ac

X₆ = -CO₂H; -NHSO₂CH₃; -NHP(O)(OBn)₂;
-NHP(O)(OH)₂; -OP(O)(OBn)₂; or
-OP(O)(OH)₂.

in a pharmaceutically acceptable carrier.

8. The pharmaceutical composition according to claim 7 wherein said compound is

selected from the group consisting of: (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-5-(O-2-acetic acid)-hydroxy-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-7-(O-2-acetic acid)-hydroxy-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-7-(N-methanesulfonamido)-amino-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-5-(N-methanesulfonamido)-amino-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-5-(N-2-acetic acid)-carboxamido-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-5-(N-2-acetic acid)-sulfonamido-2-(1-pyrrolidinyl)naphthyl]acetamide; (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-7-(N-2-acetic acid)-carboxamido-2-(1-pyrrolidinyl)naphthyl]acetamide; and (±)-2-(3,4-dichlorophenyl)-N-methyl-N-1-[1,2,3,4-tetrahydro-7-(N-2-acetic acid)-sulfonamido-2-(1-pyrrolidinyl)naphthyl]acetamide.

9. The pharmaceutical composition according to claim 7 wherein said compound is selected from the group consisting of:

2-{7-[(±)-trans-1-(N-3,4-dichlorophenylacetamido-N-methylamino)-2-(1-pyrrolidinyl)-1,2,3,4-tetrahydronaphthoxy]}acetic acid;

2,2-Diphenyl-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-methoxy-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2,2-Diphenyl-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-hydroxy-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(2-Nitro-4,5-dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-nitro-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-nitro-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-amino-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(4-Methylsulfonylphenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-nitro-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-[1-pyrrolidinyl]-7-[N,N-bis-(t-butoxycarbonylmethyl)-amino]-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-[1-pyrrolidinyl]-7-[N,N-bis-(carboxymethyl)amino]-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-[1-pyrrolidinyl]-7-[N,N-bis-(ethoxycarbonylmethyl)-amino]-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-(N-diethylphosphoramidato-amino)-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-[1-pyrrolidinyl]-7-[N-2-(diethylphosphoryl)ethyl-amino]-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-6-methoxy-7-(N-benzyl-N-methylaminosulfonyl)-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(3,4-Dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-7-(N-benzyl-N-methylaminosulfonyl)-1,2,3,4-tetrahydronaphth-1-yl]acetamide;

2-(2-Nitro-4,5-dichlorophenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-indan-1-yl]acetamide;

2-(2-Nitro-4-trifluoromethylphenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-indan-1-yl]acetamide;

2,2-Diphenyl-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-indan-1-yl]acetamide; and

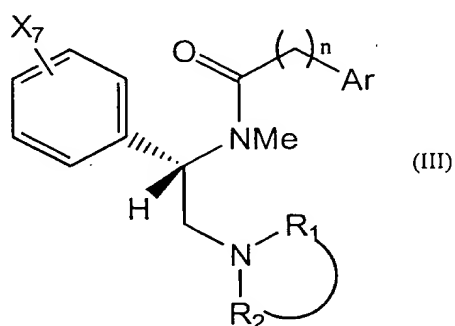
2-(4-Methylsulfonylphenyl)-N-methyl-N-[(±)-trans-2-(1-pyrrolidinyl)-indan-1-yl]acetamide.

10. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 7.

11. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 8.

12. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 9.

13. A pharmaceutical composition for the prevention or treatment of pruritus comprising
5 a compound of the formula **III** or a pharmaceutically acceptable salt thereof



wherein

$n = 1-3$;

R_1 and R_2 are independently $= CH_3$; $-(CH_2)_m$, where $m =$

4-8, $-CH_2CH(OH)(CH_2)_2-$; $-CH_2CH(F)(CH_2)_2-$;

$-(CH_2)_2O(CH_2)_2-$; or $-(CH_2)_2CH=CHCH_2-$;

Ar = unsubstituted or mono-, or di-substituted phenyl

wherein said substituents are selected from the group

consisting of halogen, OCH_3 , SO_2CH_3 , CF_3 , amino, alkyl,

and 3,4-dichloro; benzothiophenyl; benzofuranyl; naphthyl;

diphenyl methyl; or 9-fluorene;

X_7 is

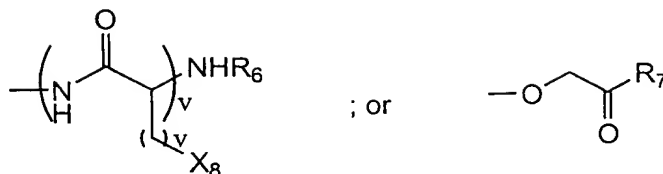
$-NHSO_2CH_3$; $-NHP(O)(OBn)_2$; $-NHP(O)(OH)_2$; $-(CH_2)_uNHSO_2CH_3$;

$-(CH_2)_uNHC(S)NHCH(CO_2H)(CH_2)_uCO_2H$; $-CONHOH$; or $-(CH_2)_uCONHOH$;

wherein

$u = 1-5$;

or X_7 is



$\text{R}_6 = \text{—H or —Ac;}$

$\text{X}_8 = \text{—CO}_2\text{H; —NHSO}_2\text{CH}_3; \text{—NHP(O)(OBn)}_2;$
 $\text{—NHP(O)(OH)}_2; \text{—OP(O)(OBn)}_2; \text{ or}$
 $\text{—OP(O)(OH)}_2;$

$\text{R}_7 = \text{—NH(CH}_2\text{)}_v\text{CO}_2\text{H; —NH(CH}_2\text{)}_v\text{CH(NH}_2\text{)(CO}_2\text{H);}$
 $\text{—NHCH(CO}_2\text{H)(CH}_2\text{)}_v\text{NH}_2; \text{—NH(CH}_2\text{)}_v\text{SO}_3\text{H;}$
 $\text{—NH(CH}_2\text{)}_v\text{PO}_3\text{H}_2; \text{—NH(CH}_2\text{)}_v\text{NHC(NH)NH}_2; \text{ or}$
 $\text{—NHCH(CO}_2\text{H)(CH}_2\text{)}_v\text{CO}_2\text{H; and}$
 $v = 1\text{--}20.$

in a pharmaceutically acceptable carrier.

- 5 14. The pharmaceutical composition according to claim 13 wherein said compound is selected from the group consisting of:

2-(3,4-dichlorophenyl)-N-methyl-N-{1-[3-(N-2-acetic acid)carboxamido]phenyl-2-(1-pyrrolidinyl)ethyl} acetamide; 2-(3,4-dichlorophenyl)-N-methyl-N-{1-[3-(N-methanesulfonamido)aminomethyl]phenyl-2-(1-pyrrolidinyl)ethyl} acetamide; 2-(3,4-dichlorophenyl)-N-methyl-N-{1-[3-(N-succinic acid-2S-thioureido)aminomethyl]phenyl-2-(1-pyrrolidinyl)ethyl} acetamide; and 2-(3,4-dichlorophenyl)-N-methyl-N-{1-[3-(N-2-acetic acid)sulfonamido]phenyl-2-(1-pyrrolidinyl)ethyl} acetamide.

- 15 15. The pharmaceutical composition according to claim 13 wherein said compound is selected from the group consisting of:

2-(3,4-Dichlorophenyl)-N-methyl-N-{[1S]-1-[N-(S-aspartic acid- α -amide-S-aspartic acid- α -amido)-3-aminophenyl]-2-[1-pyrrolidinyl]ethyl} acetamide;

- 20 2-(3,4-Dichlorophenyl)-N-methyl-N-{[1S]-1-[N-(bis-methylsulfonamido)-3-aminophenyl]-2-[1-pyrrolidinyl]ethyl} acetamide;

2-(2-Nitrophenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

- 25 2-(2-Aminophenyl)-N-methyl-N-[(1S)-1-(3-aminophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Diethyl phosphoramidate-2-aminophenyl)-N-methyl-N-[(1S)-1-(N-diethyl phosphoramidate-3-aminophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

- 30 2-(N-Bis-sulfonamido-2-aminophenyl)-N-methyl-N-[(1S)-1-(N-bis-sulfonamido-3-aminophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Nitro-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

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2-(4-Methylsulfonylphenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Butyloxycarbonyl-4-aminophenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(4-Aminophenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Bis-sulfonamido-4-aminophenyl)-N-methyl-N-[(1S)-1-(3-nitrophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Bis-sulfonamido-4-aminophenyl)-N-methyl-N-[(1S)-1-(3-aminophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Bis-sulfonamido-4-aminophenyl)-N-methyl-N-[(1S)-1-(N-diethyl phosphoramidate-3-aminophenyl)-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Nitrophenyl)-N-methyl-N-[[1S]-1-phenyl-2-[1-(3S)-(3-hydroxypyrrolidinyl)]ethyl]acetamide;

2-(2-Nitro-4,5-dichlorophenyl)-N-methyl-N-[[1S]-1-phenyl-2-[1-(3S)-(3-hydroxypyrrolidinyl)]ethyl]acetamide;

2-(4-Methylsulfonylphenyl)-N-methyl-N-[[1S]-1-phenyl-2-[1-(3S)-(3-hydroxypyrrolidinyl)]ethyl]acetamide;

2-(2-Nitro-4-trifluoromethylphenyl)-N-methyl-N-[[1S]-1-phenyl-2-[1-(3S)-(3-hydroxypyrrolidinyl)]ethyl]acetamide;

2-(2-Amino-4-trifluoromethylphenyl)-N-methyl-N-[[1S]-1-phenyl-2-[1-(3S)-(3-hydroxypyrrolidinyl)]ethyl]acetamide;

2,2-Diphenyl-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

N',N'-Diphenyl-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]urea;

2-(2-Nitrophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Nitro-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(4-Methylsulfonylphenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Methoxyphenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(3-Indolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(α,α,α -Trifluoro-p-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Nitro- α,α,α -Trifluoro-4-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(1-[4-Chlorobenzoyl]-5-methoxy-2-methyl indole)-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(4-Nitrophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(3-Nitrophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Pyridyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(3-Pyridyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-((+)-6-Methoxy- α -methyl-2-napthalene)-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(α,α,α -Trifluoro-3-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(4-Pyridyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(α,α,α -Trifluoro-2-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-((S)-(+)-4-Isobutyl- α -methylphenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(3,4,5-Trimethoxyphenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-N,N-Dimethylsulfonamido-2-aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Methylsulfonamido-2-aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Amino 4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N,N-Dimethylsulfonamido-2-amino-4,5-dichlorophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Amino, α,α,α -Trifluoro-4-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-N,N-Dimethylsulfonamido-2-amino- α,α,α -trifluoro-4-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N-Methylsulfonamido-2-amino- α,α,α -trifluoro-4-tolyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(4-Aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N,N-Dimethylsulfonamido-2-aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(N,N-Dimethylsulfonamido-2-aminophenyl)-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide;

2-(2-Hydroxyphenyl)-N-methyl-N-methyl-N-[(1S)-1-phenyl-2-(1-pyrrolidinyl)ethyl]acetamide; and

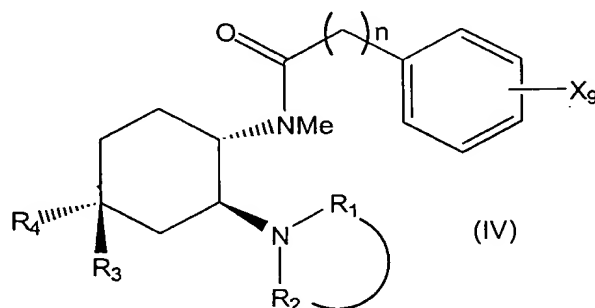
N-Methyl-N-[(1S)-1-phenyl-2-((3S)-3-hydroxypyrrolidine-1-yl)ethyl]-3,4,5-trimethoxyphenylacetamide.

16. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 13.

17. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 14.

18. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 15.

19. A pharmaceutical composition for the prevention or treatment of pruritus comprising a compound of the formula IV or a pharmaceutically acceptable salt thereof



wherein

$n = 1-3$;

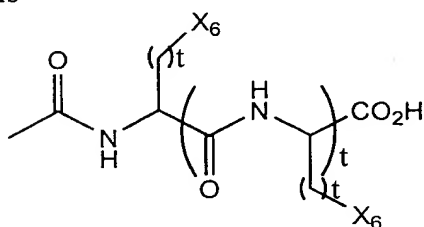
R_1 and R_2 are independently $= CH_3$; $-(CH_2)_m$, where $m = 4-8$, $-CH_2CH(OH)(CH_2)_2$; $-CH_2CH(F)(CH_2)_2$; $-(CH_2)_2O(CH_2)_2$; or $-(CH_2)_2CH=CHCH_2$;

R_3 and R_4 are independently H; OCH_3 ; alkyl; or $c-O(CH_2)_2$;

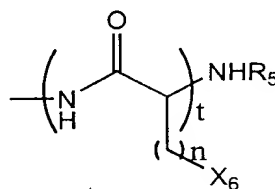
5 $X_9 = 1-4$ substituents selected from the groups consisting of

-halogen, $-CF_3$; $-OCH_3$; $-SO_2NH(CH_2)_qCO_2H$; $-CONH(CH_2)_qCO_2H$;
 $-NH_2$; $-NHSO_2CH_3$; $-NHP(O)(OBn)_2$; $-NHP(O)(OH)_2$; $NH(CH_2)_qCO_2H$; $-SO_2CH_3$;
 $-OP(O)(OBn)_2$; $-OP(O)(OH)_2$; $-CO_2H$; $-O(CH_2)_qCO_2H$; $-O(CH_2)_qSO_3H$,
 $-O(CH_2)_qOPO_3H_2$; wherein
 $q = 1-20$;

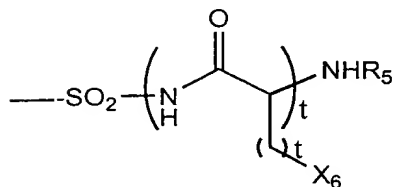
or X_9 is



; or



; or



15 wherein

$t = 1-20$;

$R_5 = -H$ or $-Ac$;

$X_6 = -CO_2H$; $-NHSO_2CH_3$; $-NHP(O)(OBn)_2$;
 $-NHP(O)(OH)_2$; $-OP(O)(OBn)_2$; or
 $-OP(O)(OH)_2$.

in a pharmaceutically acceptable vehicle.

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20. The pharmaceutical composition according to claim 19 wherein said compound is selected from the group consisting of:

(-)-(5 α ,7 α ,8 β)-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro-[4,5]dec-8-yl]-3-(N-methanesulfonamido)aminophenylacetamide; (-)-(5 α ,7 α ,8 β)-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro-[4,5]dec-8-yl]-3-(N-2-acetic acid)sulfonamidophenylacetamide; and (-)-(5 α ,7 α ,8 β)-N-methyl-N-[7-(1-pyrrolidinyl)-1-oxaspiro-[4,5]dec-8-yl]-3-(N-2-acetic acid)carboxamidophenylacetamide.

21. The pharmaceutical composition according to claim 19 wherein said compound is selected from the group consisting of:

(\pm)-*trans*-2-Nitro-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Amino-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Nitro-4,5-dichloro-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Amino-4,5-dichloro-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Methanesulfonamido-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

N-[2-(\pm)-*trans*-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamido]glycine Hydrochloride;

(\pm)-*trans*-4-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Nitro-4-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Amino-4-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Bismethanesulfonamido-4-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(\pm)-*trans*-2-Methanesulfonamido-4-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

N-[2-(±)-*trans*-4-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamido]glycine Hydrochloride;

(±)-*trans*-3-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-5-Nitro-3-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-2-Nitro-3-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-2-Trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-4-Nitro-2-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-4-Amino-2-trifluoromethyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]-phenylacetamide Hydrochloride;

(±)-*trans*-N-Methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]2,2-diphenylacetamide Hydrochloride; and

(±)-*trans*-4-Methylsulfonyl-N-methyl-N-[2-(1-pyrrolidinyl)cyclohexyl]phenylacetamide Hydrochloride.

22. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 19.

23. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 20.

24. A method for the prevention or treatment of pruritus in a patient comprising administering to said patient an effective amount of a composition according to claim 21.